Patient satisfaction with dabigatrean and warfarin for stroke prevention in atrial fibrillation: Taiwan PASSION study

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Abstract

Background: Patient satisfaction with oral anticoagulant (OAC) therapy is an important metric of care quality and has been associated with higher medication persistence. Among OACs, dabigatran has been shown to be non-inferior to vitamin K antagonists (VKAs) with increased ease of use for stroke prevention in patients with atrial fibrillation (AF). In this study, we sought to evaluate the expectations, convenience, and satisfaction of Taiwanese AF patients on dabigatran and VKA therapies as well as associated clinical outcomes.

Methods: Patients with AF (paroxysmal, persistent, or permanent) receiving OAC medication from outpatient facilities were enrolled in 24 hospitals across Taiwan. Cohort A consisted of 139 patients switched from VKA to dabigatran, while cohort B was comprised of 1113 patients on newly initiated OAC therapy (VKA, 54). The Perception of Anticoagulant Treatment Questionnaire was distributed, and responses on a five-point Likert scale were aggregated and analyzed across demographic groups.

Results: In cohort A, convenience and satisfaction scores continued to increase at follow-up and significantly higher, compared to baseline, but both treatments scored similarly in cohort B. In cohort B, the two highest expectation scores were that the OAC would be "easy to take" and could be "taken independently." On the other hand, the patients were relatively less concerned about the side effects and cost of therapy before taking the OAC. For dabigatran-receiving patients, there were 1.1 stroke-related events per 100 patient-years and 3.0 bleeding-related events per 100 patient-years.

Conclusion: In Taiwanese patients with AF and initially treated with VKA, switched to dabigatran resulted in higher convenience and treatment satisfaction. For those patients on newly initiated OAC treatment, VKA and dabigatran convenience and satisfaction scores were similar.

Keywords: Convenience; Dabigatran; Patient expectation; Satisfaction; Warfarin

1. INTRODUCTION

Atrial fibrillation (AF) is a common cardiac arrhythmia and leading cause of stroke.[1,2] As such, patients with AF are often administered oral anticoagulants (OACs) for stroke prevention. Traditional OACs, such as warfarin, act as vitamin K antagonists (VKAs), but in recent years, non-vitamin K antagonist oral anticoagulants (NOACs) have been developed. Randomized controlled trials showed that compared to warfarin, NOACs are non-inferior in efficacy and safety. Additionally, patients often find NOACs to be more convenient than VKAs, as they do not require periodic blood tests to monitor clotting ability.[3]

The orally administered direct thrombin inhibitor, dabigatran, was the first NOAC available on the market. Dabigatran was approved after evaluation in the pivotal Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) trial,[4] and since its clinical introduction, usage of NOACs as a replacement for warfarin has increased rapidly throughout the world.[5,6] Despite widespread application of OAC therapies, only limited data existed regarding the patient's perspective of convenience, burden of disease and treatment, and satisfaction with therapy in the real world. Such information in different clinical settings can be collected using established evaluation tools. Such information in different clinical settings can be collected using established evaluation tools.[7,8] To make assessments of patient expectations

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and satisfaction with anticoagulant therapies, the Perception of Anticoagulant Treatment Questionnaire (PACT-Q), a valid, reliable, and widely used tool[9] was applied in this study. We sought to assess expectations, convenience, and satisfaction with dabigatran therapy as well as clinical outcomes for patients with AF in Taiwan.

2. METHODS

2.1. Study Design and Trial Population

A noninterventional, multicenter, quantitative descriptive observational study on patients with nonvalvular AF was conducted. The study included two cohorts of patients being treated with OACs for stroke prevention. Cohort A consisted of patients who switched from VKA to dabigatran. Cohort B was comprised of patients that were newly initiated on dabigatran or VKA. All participants provided written informed consent before enrollment. Patients who met all of the following criteria were eligible for inclusion: (1) age at least 20 years; (2) previous, persistent, permanent, or paroxysmal non-valvular AF; (3) planned long-term use of an OAC. Patients using anticoagulation therapies for other conditions (eg, prosthetic valves, venous thromboembolism, or mitral stenosis) were not eligible. Other key exclusion criteria were any contraindications to the use of dabigatran or VKA and participation in any other clinical trial or AF-related registry. The study was registered in www.ClinicalTrials.gov and the identifier was NCT03187197. This study was independently approved by all the Institutional Review Board of 24 sites, including MacKay Memorial Hospital.

2.2. Assessment and Study Endpoints

All patients were evaluated three times, first in a baseline exam, then in a second visit (V2) and third visit (V3). V2 was arranged 30 to 45 days after baseline, and V3 was 150 to 210 days after baseline. The PACT-Q was used to assess expectations, convenience, and satisfaction with anticoagulant treatment. In cohort

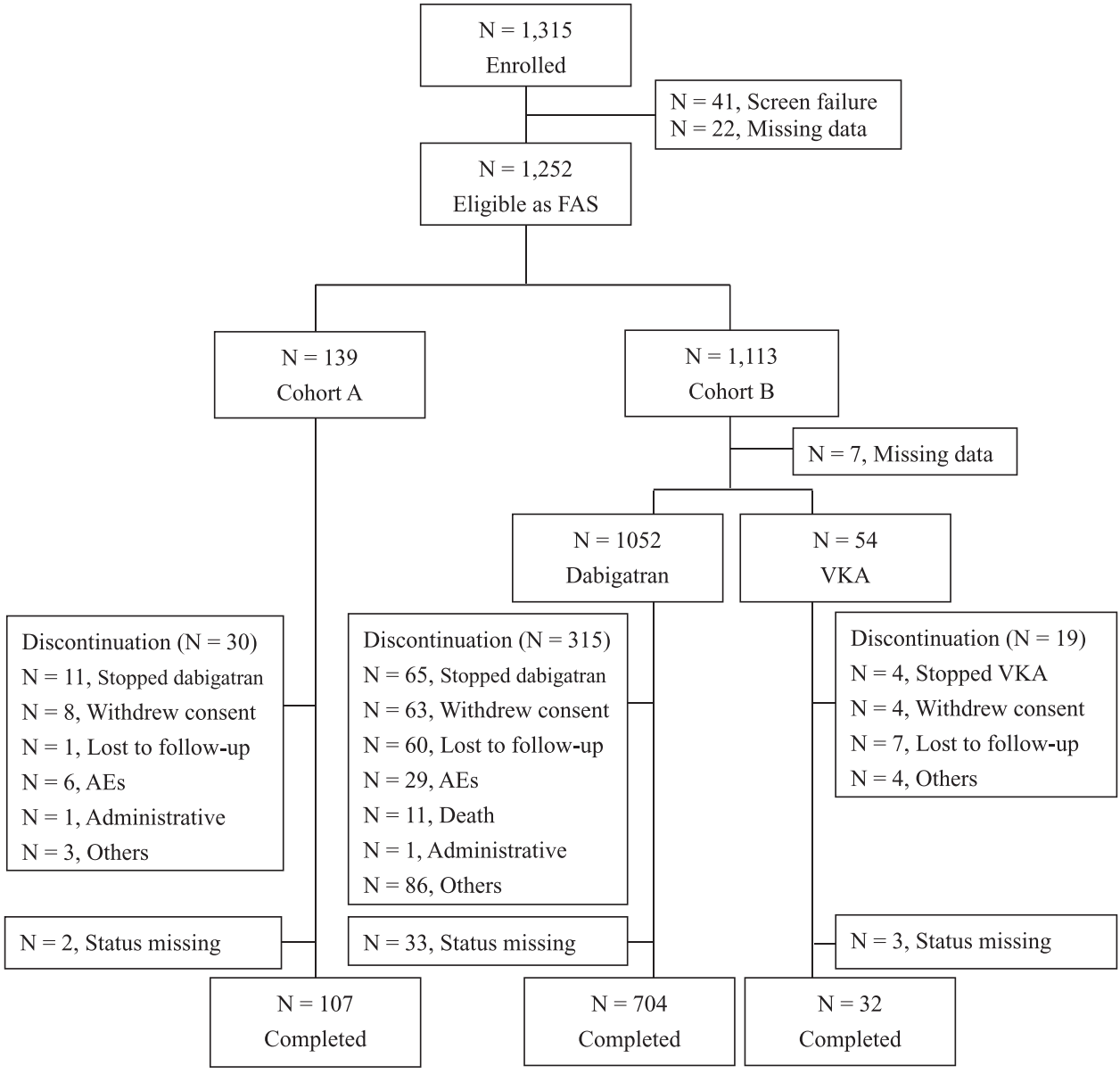

Fig. 1 Flow chart of overall study population of cohort A & B.

A, Part 2 of PACT-Q (PACT-Q2) was completed at baseline, V2, and V3. In cohort B, Part 1 of the PACT-Q (PACT-Q1) was done at baseline, and PACT-Q2 was completed at V2 and V3.

The primary efficacy endpoint for cohort A was the mean PACT-Q2 scores at V2 and V3 compared to those at baseline. The primary efficacy endpoint for cohort B was the mean PACT-Q2 scores at V2 and V3 compared between patients receiving dabigatran and VKA. The mean PACT-Q2 scores at V3 compared to V2 were a secondary endpoint for cohort A. The secondary endpoint for cohort B was the mean PACT-Q1 scores at baseline.

2.3. Questionnaire

The PACT-Q1 questionnaire assesses patient expectations for anticoagulant treatment according to seven questions. The PACT-Q2 questionnaire includes a total of 20 questions: eleven assess treatment convenience; two evaluate burden of disease and treatment; seven are related to treatment satisfaction. Based on the aggregated responses, we calculated global dimension scores (maximum 100) for convenience and satisfaction.

2.4. Statistical Analyses

The main analysis population consisted of all eligible patients (ie, all patients who signed the informed consent, fulfilled all inclusion criteria, and did not meet any exclusion criteria). In addition, eligible patients were categorized into cohorts A and B, and subcategorized as dabigatran initiators or VKA initiators. The two cohorts and two subgroups were compared in PACT-Q analyses. Analytic specifications, including tables and listings, are detailed in a statistical analysis plan that is separate from the full study protocol. Statistical analyses of all data were performed using the latest version of SAS statistical software (SAS Institute, Cary, NC). All statistical tests were two-sided, and statistical significance was set at $p < 0.05$. The continuous variables were analyzed by two-sample T-test and the categorical variables were analyzed by Chi-square test.

2.5. Clinical Outcomes

Clinical outcomes were also evaluated, including the event rate (stroke) and bleeding rate (any bleeding). The event and bleeding rates found in this study were compared with those in previous reports.

3. RESULTS

3.1. Patient Demographic and Baseline Characteristics

Between July 23, 2017 and January 11, 2019, a total of 1315 patients were screened and 1252 patients were enrolled. Cohort A consisted of 139 patients, and 1113 patients were assigned to cohort B, with 1052 patients on dabigatran and 54 patients on VKA (data were missing from seven patients; Fig. 1). The demographic features and baseline characteristics, including stroke risk, bleeding risk, and history of VKA are summarized in Table 1. For the patients newly initiated OAC (cohort B), those on dabigatran were older than those on VKA (71.5 ± 13.08 vs 67.1 ± 12.88 years, $p < 0.05$). In addition, CHA_2DS_2-VASc score was higher in the dabigatran users, compared to VKA users (3.4 ± 1.62 vs 2.5 ± 1.88, $p < 0.05$). The patients had several comorbidities at baseline without significant difference between groups (Table 2). The discontinuation rate of cohorts A and B were 21.5% and 30.0%, respectively.

3.2. Convenience and Satisfaction in Cohort A

The PACT-Q global dimension score for convenience was 86.9 at baseline, 91.7 at V2, and 95.2 at V3 (Fig. 2A); the PACT-Q global dimension score for satisfaction was 64.3 at baseline, 68.1 at V2, and 72.5 at V3 (Fig. 2B). Both convenience and

Table 1

Patient demographics and characteristics at baseline[a]

			Cohort B	
	Overall (N = 1245)	Cohort A (N = 139)	Dabigatran (N = 1052)	VKA (N = 54)
Age (y)	71.0 ± 13.44	68.4 ± 15.65	71.5 ± 13.08	67.1 ± 12.88
Male, n (%)	740 (59.5)	82 (59.4)	621 (59.1)	37 (68.5)
Height (cm)	161.3 ± 8.92	162.8 ± 8.45	161.0 ± 8.97	163.2 ± 8.72
95% CI	160.8-161.9	161.2-164.3	160.4-161.6	160.6-165.9
Weight (kg)	67.8 ± 14.38	68.7 ± 15.18	67.6 ± 14.17	70.3 ± 16.28
95% CI	67.0-68.7	66.0-71.3	66.7-68.5	65.4-75.1
BMI (kg/m^2)	26.0 ± 4.78	25.7 ± 4.76	26.0 ± 4.78	26.2 ± 4.95
95% CI	25.7-26.3	24.8-26.6	25.7-26.3	24.7-27.7
BMI category, n (%)				
<18.5 kg/m^2	22 (2.1)	4 (3.4)	16 (1.8)	2 (4.4)
18.5-24 kg/m^2	351 (33.6)	43 (36.1)	295 (33.5)	13 (28.9)
24-27 kg/m^2	328 (31.4)	34 (28.6)	277 (31.5)	17 (37.8)
≥27 kg/m^2	343 (32.9)	38 (31.9)	292 (33.2)	13 (28.9)
CHA_2DS_2-VASc (points)[a]	3.3 ± 1.64	3.1 ± 1.60	3.4 ± 1.62	2.5 ± 1.88[b]
95% CI	3.2-3.4	2.8-3.4	3.2-3.5	1.9-3.1
HAS-BLED (points)	2.1 ± 1.08	2.2 ± 1.04	2.0 ± 1.03	2.3 ± 2.21
95% CI	1.9-2.2	2.0-2.4	1.8-2.2	0.2-4.3
Previous VKA (y)		2.7 ± 2.24		
Median		2.2		
95% CI	—	(2.2-3.1)	—	—
Able to read or write, n (%)	1064 (86.7)	127 (93.4)	889 (85.7)	48 (88.9)
Alcohol (active/past), n (%)	11 (0.9)	0 (0.0)	9 (0.9)	2 (3.9)

Cohort A: switched from VKA to dabigatran; cohort B: newly initiated on dabigatran or VKA.

BMI = body mass index; CI = confidence interval; HAS-BLED = Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly; VKA = vitamin K antagonist.

[a]Mean ± SD, unless mentioned else. Missing data were excluded from the analysis.

[b]$p < 0.05$ between dabigatran and VKA in cohort B.

Table 2

Patient comorbidities at baseline

Diagnosis, n (%)	Overall (N = 1245)	Cohort A (N = 139)	Cohort B	
			Dabigatran (N = 1052)	VKA (N = 54)
Diabetes	360 (29.7)	37 (26.8)	308 (30.0)	15 (29.4)
Hypertension	797 (65.5)	83 (60.1)	683 (66.5)	31 (60.8)
Ischemic heart disease	279 (23.2)	30 (22.1)	237 (23.3)	12 (23.5)
Congestive heart failure	351 (28.9)	58 (42.0)	281 (27.4)	12 (23.5)
Left ventricular dysfunction	78 (6.4)	12 (8.7)	63 (6.1)	3 (5.9)
Stroke	105 (8.6)	11 (8.0)	92 (9.0)	2 (3.9)
Transient ischemic attack	37 (3.0)	4 (2.9)	32 (3.1)	1 (2.0)
Thromboembolism	35 (2.9)	5 (3.6)	28 (2.7)	2 (3.9)
Vascular disease	123 (10.1)	11 (8.0)	104 (10.1)	8 (15.7)
Myocardial infarction	49 (4.0)	6 (4.4)	41 (4.0)	2 (3.9)
Peripheral artery disease	16 (1.3)	1 (0.7)	13 (1.3)	2 (3.9)
Abnormal renal function[a]	127 (10.5)	18 (13.0)	97 (9.5)	12 (23.5)
Abnormal liver function[b]	86 (7.1)	9 (6.5)	70 (6.8)	7 (14.0)
Bleeding[c]	41 (3.4)	1 (0.7)	38 (3.7)	2 (3.9)
Chronic dialysis	5 (0.4)	0 (0.0)	1 (0.1)	4 (7.4)
Medication predisposing to bleeding[d]	169 (13.6)	23 (16.5)	145 (13.8)	1 (1.9)

Cohort A: switched from VKA to dabigatran; cohort B: newly initiated on dabigatran or VKA.

Missing data were excluded from the analysis.

NVAF = nonvalvular atrial fibrillation; VKA = vitamin K antagonist.

[a]Abnormal renal function, such as a presence of chronic dialysis, renal transplantation, or abnormal serum creatinine value (creatinine > 1.2 mg/dL).

[b]Abnormal liver function, such as chronic hepatic disease (eg, cirrhosis) or biochemical evidence of significant hepatic derangement (eg, bilirubin > 2 × upper limit of normal, in association with AST/ALT/AP > 3 × upper limit normal).

[c]Bleeding: Any prior bleeding history or predisposition to bleeding (eg, anemia).

[d]Medication predisposing to bleeding, that is, any antiplatelet agent.

satisfaction improved at follow-up. In patients who were swifted from VKA to dabigatran, the convenience score significantly increased by 4.8 and 8.3 compared to baseline (at 1 month and 6 months, respectively; $p < 0.0001$). Meanwhile, the satisfaction scores increased by 3.8 and 8.2 (at 1 month and 6 months, respectively; $p < 0.01$).

3.3. Expectations, Convenience and Satisfaction in Cohort B

In cohort B, the two highest expectation scores were that the OAC would be "easy to take" and "could be taken independently." On the other hand, the patients were relatively less concerned about the side effects and cost of therapy before taking the OAC. At follow-up visits, the PACT-Q global dimension scores for VKA convenience were 94.3 at V2 and 94.3 at V3. Comparatively, the PACT-Q global dimension scores for dabigatran convenience were 92.4 at V2 and 93.9 at V3 (Fig. 3). No significant differences were found in global convenience scores between the dabigatran and VKA users. The PACT-Q global dimension scores for VKA satisfaction were 67.3 at V2 and 75.1 at V3 (Fig. 4), while dabigatran scores were 70.2 at V2 and 73.9 at V3. No significant differences were found in global satisfaction scores between the dabigatran and VKA users.

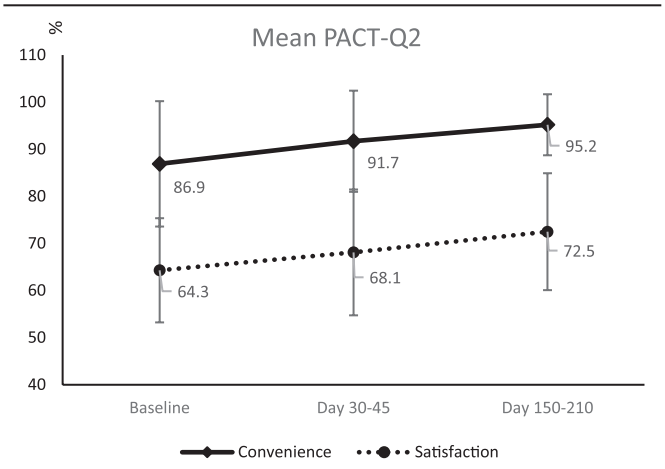

Fig. 2 The PACT-Q global dimension score for convenience & satisfaction in cohort A.

3.4. Comparison of Vitamin K Antagonist Convenience and Satisfaction Between Cohorts A and B

The PACT-Q2 convenience scores for VKA at baseline were 94.3 in cohort B and 86.9 in cohort A (Table 3). The PACT-Q2 satisfaction scores for VKA in cohort B was 75.1 and in cohort A was 64.3 (Table 4). Compared with V3 of cohort B, both convenience and satisfaction scores were significantly lower in V1 of cohort A.

3.5. Clinical Outcomes

At the end of the study, we also examined the rates of stroke and bleeding occurrence in the study population. There were five-stroke events in patients on dabigatran during 6 months of follow-up. To further evaluate safety, we also assessed bleeding-related events, which occurred at 3.0 per 100 patient-years in our study population (Table 5).

4. DISCUSSION

Since NOACs make anticoagulant therapy easier to implement for AF patients, the prescription rate of these drugs has steadily increased around the world.[10] It is therefore becoming more and more essential to understand the patient's perception of NOACs in real-world settings. The aim of this study was to evaluate the expectations, convenience, and patient

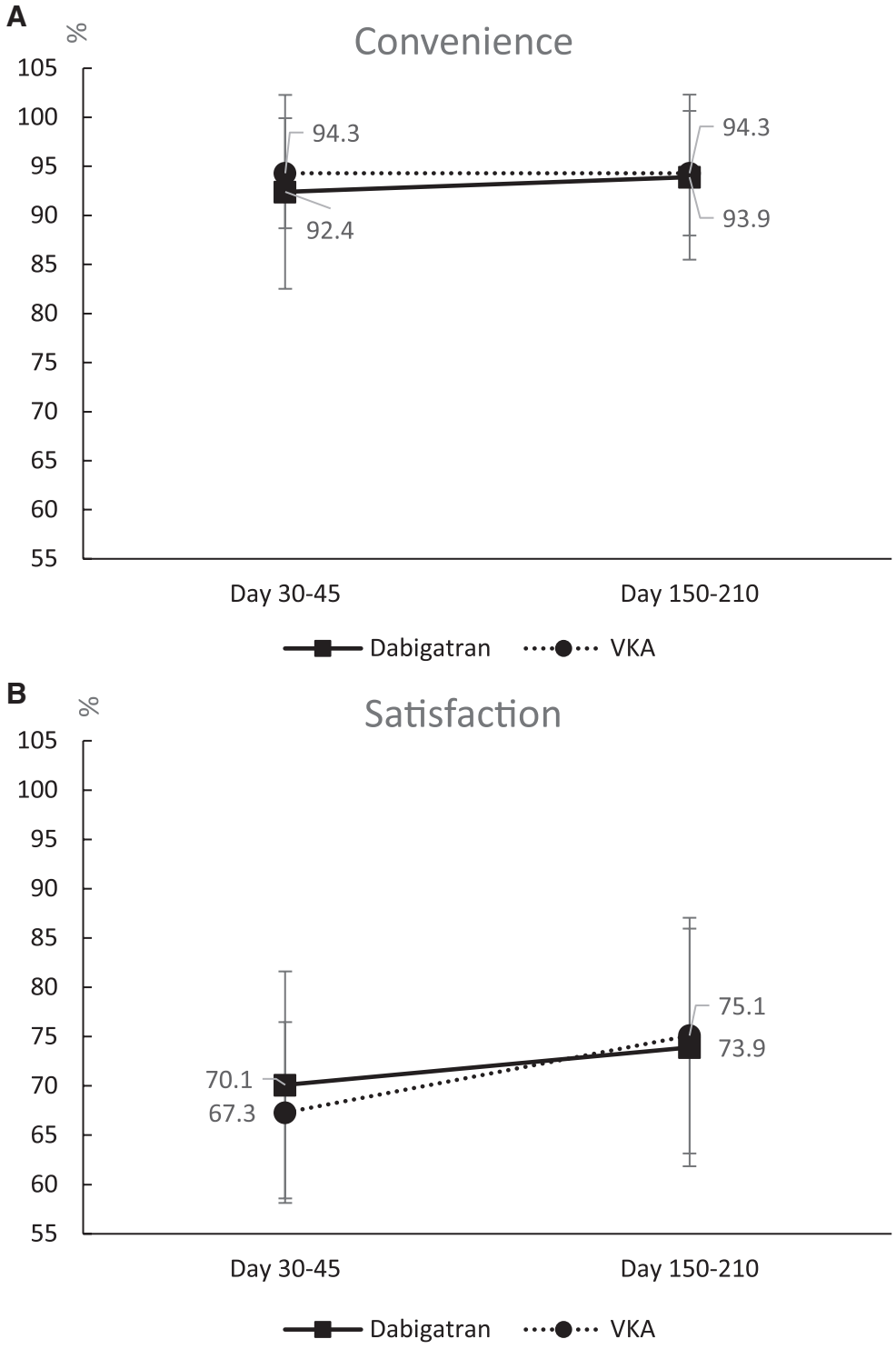

Fig. 3 The PACT-Q global dimension scores for (A) convenience & (B) satisfaction in cohort B.

satisfaction with dabigatran therapy and clinical outcomes among patients with AF. In the cohort of patients who had switched from VKA to dabigatran, the global convenience and satisfaction scores steadily increased at each subsequent visit. The patients in this cohort had experienced both VKA and dabigatran, and the results clearly indicate that they prefer the NOAC over VKA.

For patients who had newly initiated anticoagulant therapy, our study showed the two highest expectation scores for OACs were for easy to take and could be taken independently. Similar results were also shown by Gospos and Bernaitis,[9] Obamiro et al,[11] Cajfinger et al,[12] Smet et al,[13] and Larochelle et al,[14] who also utilized the PACT-Q1 survey and reported the highest mean expectation score for OACs was easy to take. Also, compared

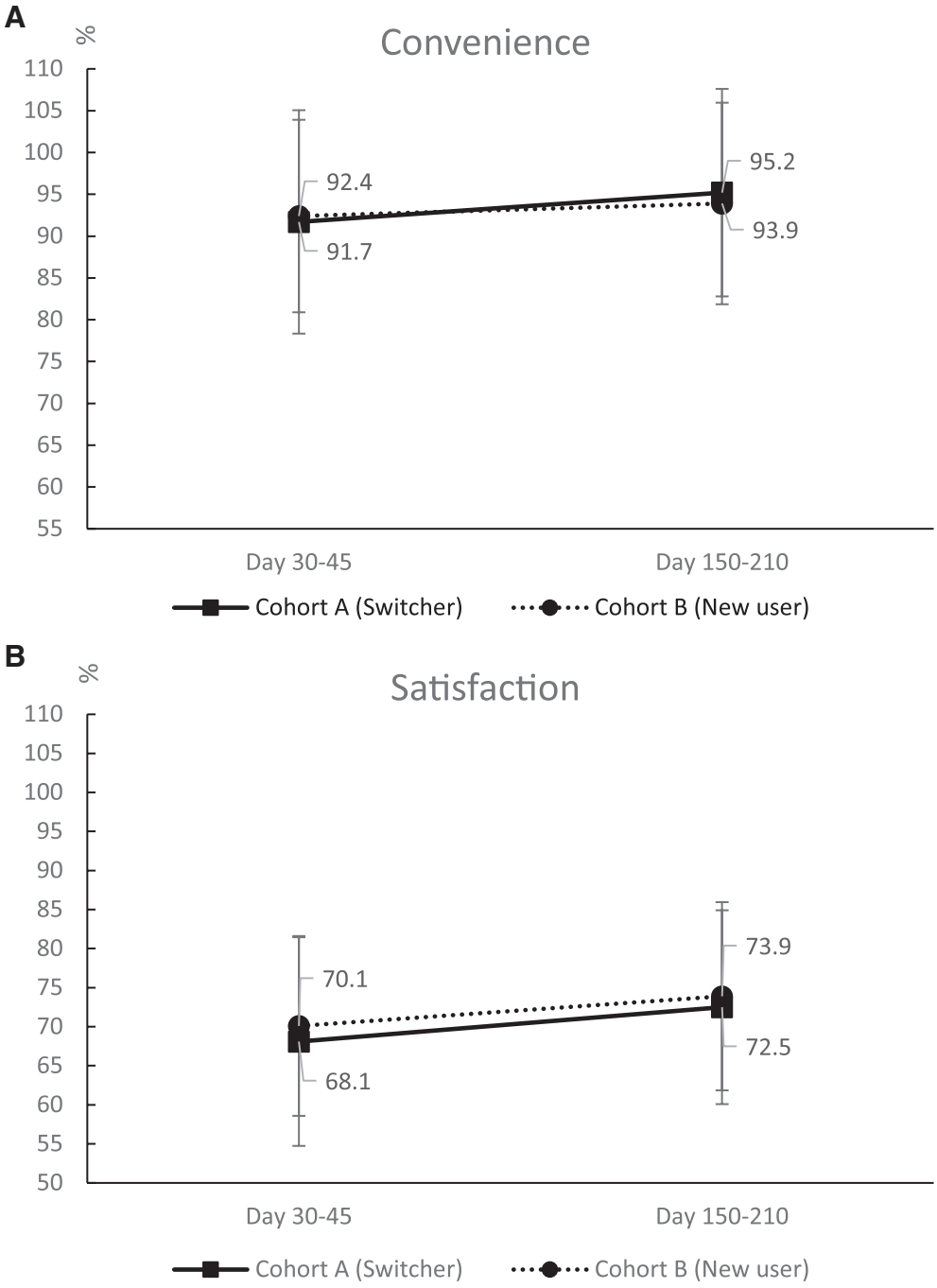

Fig. 4 The PACT-Q global dimension scores for (A) convenience (B) satisfaction in the switcher & new user of dabigatran.

with earlier studies, our participants were less concerned about the cost of anticoagulant therapy. In Taiwan, both VKA and NOAC are reimbursable by the National Health Insurance, and the out-of-pocket cost paid by patients is similar for both drugs; hence, patients in Taiwan tend to be more concerned about aspects other than the cost.

Cohort B patients scored VKA and dabigatran similarly for convenience and satisfaction. This finding was in accordance with Okumura et al.[15] who reported no difference in global satisfaction scores between NOAC and VKA, whereas Goette et al.[16] found satisfaction scores of 65.8 for patients taking edoxaban and 70.6 for those on enoxaparin and VKA. In contrast, other studies reported higher satisfaction with NOAC therapy than VKA.[17,18] This variation between studies may be explained by differences in health care and health insurance systems at the study sites. Alternatively, our result might be due to the fact that in cohort B, we only had 54 patients in the VKA group, which might not accurately reflect the whole population.

In the present study, the global convenience score for dabigatran was 92 to 95. Conversely, lower convenience scores have been reported by Gospos and Bernaitis[19] at 68.9, Cajfinger et al[12] at 79.7, Smet et al[13] at 86.7, and Obamiro et al[11] at 88.4. In addition to variation derived from the health care system, the variation of medication evaluated among the studies may also

Table 3

Summary of PACT-Q2 score for convenience in VKA users

Characteristics	Cohort A at baseline (N = 139)	Cohort B: VKA at V3 (N = 54)	*p*
PACT-Q2 score: convenience			
N	136	34	
Mean ± SD	86.9 ± 13.31	94.3 ± 6.35	<0.0001[a]
Median	91.5	95.4	
Range	49.2-100.0	69.2-100.0	
IQR (Q1-Q3)	16.9 (80.0-96.9)	9.2 (90.8-100.0)	
95% CI	84.6-89.1	92.0-96.5	
Missing	3	20	

CI = confidence interval; IQR = interquartile range; PACT-Q2 = Part 2 of Perception of Anticoagulant Treatment Questionnaire; VKA = vitamin K antagonist.
[a]Paired *t* test.

Table 4

Summary of PACT-Q2 score for satisfaction in VKA users

Characteristics	Cohort A at Baseline (N = 139)	Cohort B: VKA at V3 (N = 54)	*p*
PACT-Q2 score: satisfaction			
N	138	34	
Mean ± SD	64.3 ± 11.06	75.1 ± 11.95	<0.0001[a]
Median	65.7	74.3	
Range	(40.0-97.1)	(54.3-100.0)	
IQR (Q1-Q3)	14.3 (57.1-71.4)	11.4 (68.6-80.0)	
95% CI	(62.5-66.2)	(71.0-79.3)	
Missing	1	20	

CI = confidence interval; IQR = interquartile range; PACT-Q2 = part 2 of Perception of Anticoagulant Treatment Questionnaire; VKA = vitamin K antagonist.
[a]Paired T test.

Table 5

Efficacy and safety outcomes for patients receiving dabigatran

Events	Overall (N = 1191)	Per 100 patient-years	Switched from VKA (N = 139)	Newly initiated (N = 1052)
Stroke	5 (0.4%)	1.1	2 (1.4%)	3 (0.3%)
Any bleeding	11 (0.9%)	3.0	2 (1.4%)	9 (0.9%)

VKA = vitamin K antagonist.

explain the difference in convenience scores.[20] Our study is the first to compare only dabigatran and VKA, while other studies may include several NOACs. Importantly, our study also showed the global convenience score was maintained during follow-up.

To understand the differences of convenience and satisfaction between long-term and short-term VKA users, we compared the scores at baseline of cohort A (used VKA for more than 2 years) with those of VKA users at V3 in Cohort B (used VKA for 60 days). The convenience score for VKA in V3 of cohort B was 94.3, and the score at baseline of cohort A was 86.9. The satisfaction score for VKA in V3 of cohort B was 75.1, and the score at baseline of cohort A was 64.3, each pair of reached statistical difference. These results imply that although VKA initial users were with fair convenience and satisfaction scores, both of the scores drop over time.

In the present study, the rate of stroke-related events per 100 patient-years was 1.1, which is similar to previous real-world data for dabigatran; the GLORIA-AF[21] reported 0.65 and RE-LY EU label analysis[22] reported 1.10. With regard to safety, our data showed consistency with other studies. Bleeding-related events occurred at a rate of 3.0 per 100 patient-years in our data (Table 3), comparable to this finding, major bleeding events in GLORIA-AF[21] were reported 0.97 per 100 patient-years and RE-LY EU label analysis[22] reported 3.02 per 100 patient-years in major bleeding event. In the present study, real-world data from Taiwan revealed that dabigatran was associated with low rates of bleeding and stroke, comparable to the results of previous global studies.

The present study had certain limitations. For example, the study used an open-label design and enrolled patients were not randomized. However, only an observational study can provide a real-life assessment of treatment satisfaction. Another limitation of the study is that the investigators may have been more willing to enroll patients with good health to participate in the trial. As a result, patient selection bias may limit the generalizability of the study results. Finally, our cohort B contained a relatively small sample size of individuals who initiated with VKA. This small sample size may influence the ability to adequately control for confounding factors.

In conclusion, this study represents the largest real-world evaluation of the expectations, convenience, and patient satisfaction with dabigatran and VKA therapy, as assessed by questionnaires administered over the course of 6 months to patients with AF who received NOAC or VKA for stroke prevention. This trial is also the only study that administered questionnaires multiple times to provide more information about patient perception during the follow-up period. In Taiwanese patients with AF and initially treated with VKA, switched to dabigatran resulted in higher convenience and treatment satisfaction. For those patients on newly initiated OAC treatment, VKA and dabigatran convenience and satisfaction scores were similar. These features regarding OAC plus low event rates of dabigatran are compatible with global data.

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